IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	**US 6,143,771**
Issued:	**November 7, 2000**
To:	**Per Lennart Lindberg; Sverker von Unge**
For:	**COMPOUNDS**

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. 1.8
I hereby certify that this paper is being facsimile transmitted to the U.S. Patent and Trademark Office on January 27, 2006 at the facsimile number 571-273-8300.

John M. Genova — 32,224
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Signature — January 27, 2006
Date of Signature

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9 Pages

REQUEST FOR RECONSIDERATION OF FINAL DETERMINATION

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Sir:

On July 28, 2005, the United States Patent and Trademark Office ("USPTO") issued a Notice of Final Determination (the "Notice") alleging that US 6,143,771 (the "'771 patent") is not eligible for patent term extension under 35 U.S.C. § 156 based upon the approval of NEXIUM® I.V. Acknowledging that the determination of eligibility of the '771 patent turns on the requirement that the FDA approval of NEXIUM I.V is for the first permitted commercial marketing or use of the product under 35 U.S.C. § 156(a)(5)(A), the USPTO turned to Pfizer, Inc. v. Dr. Reddy's Labs., 359 F.3d 1361 (Fed. Cir. 2004) for guidance on what constitutes a "product" as defined by 35 U.S.C. § 156(f). In the context of enforcement under 35 U.S.C. § 56(b) (the "rights derived section"), Pfizer gives "product" a broad scope covering an entire active moiety including amlodipine *and* its salts, amlodipine besylate and amlodipine maleate.

In its denial of eligibility, however, the USPTO failed to consider the meaning of "product" in the context of eligibility under 35 U.S.C. § 156(a) (the "eligibility section"), as construed by the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") in Glaxo Operations UK Ltd. v. Quigg, 894 F.2d 392 (Fed. Cir. 1990) and, without any proper basis, declared Glaxo overruled by Pfizer. The USPTO reached this conclusion by suggesting that Glaxo and Pfizer were inconsistent:

> Eligibility for patent term extension must be consistent with the rights derived from a patent term extension. Accordingly, if the rights derived from the extension of a patent based upon the regulatory approval of a salt encompass other compounds within the same active moiety, then extension based upon subsequent approvals of other compounds within the same active moiety must be barred. As Pfizer suggests this result, Glaxo must be treated as overruled . . . .

(Notice of Final Determination ("Notice") at 3.) The application for patent term extension of the '771 patent was therefore denied because the active moiety in NEXIUM I.V., esomeprazole, was previously approved in NEXIUM® (esomeprazole magnesium) and hence esomeprazole sodium did not constitute the first commercial marketing or use as required by 35 U.S.C. § 156(a)(5)(A).

It is respectfully submitted that the USPTO misinterpreted and misapplied both Federal Circuit law and the statutory provisions of 35 U.S.C. § 156 in denying the application for patent extension of the '771 patent for the following reasons:

(1) Glaxo cannot be overruled by Pfizer and remains binding precedent;

(2) Glaxo is more applicable to the USPTO's review of the instant application because Glaxo applies to eligibility and Pfizer, to enforcement, which the Federal Circuit has recognized as different issues with different analyses; the circumstances surrounding the patent term extension application for the '771 patent are similar to the facts of Glaxo and distinguishable from the facts of Pfizer; and

(3) The policy rationale of the Hatch-Waxman Act[1] favors granting patent term extension for the '771 patent.

In view of the applicable statutory provisions as interpreted by the Federal Circuit, the '771 patent in connection with NEXIUM I.V. (esomeprazole sodium) should be eligible for patent term restoration under 35 U.S.C. § 156.

1. Relevant Facts

AstraZeneca AB ("AstraZeneca") timely filed in the USPTO an application for extension of the patent term of the '771 patent under 35 U.S.C. § 156 on May 25, 2005. Extension was sought based upon the pre-market review of NEXIUM I.V. (esomeprazole sodium) for injection under § 505(b) of the Federal Food, Drug, and Cosmetic Act. AstraZeneca submitted NDA 21-689 to the U.S. Food and Drug Administration ("FDA") for NEXIUM I.V. on September 10, 2003, and the FDA approved it for commercial use and sale on March 31, 2005. The applicable IND, IND 64,865, was submitted on May 22, 2002.

The '771 patent, which issued on November 7, 2000, and is assigned to AstraZeneca, contains claims that are directed to pharmaceutical formulations for parenteral administration and methods of inhibiting gastric acid secretion and treating gastrointestinal inflammatory disease comprising the parenteral administration of the sodium salt of the *S*- or (-)-enantiomer of omeprazole. Thus, the claims cover the approved formulation of NEXIUM I.V. for injection after reconstitution and its method of use. The term of the '771 patent has not previously been extended and is due to expire on May 27, 2014.

2. Glaxo Remains Binding Precedent

The USPTO has failed to properly apply the binding precedent of the Federal Circuit and has instead incorrectly and without authority treated Glaxo as if overruled by Pfizer. Federal Circuit Rule 35 explicitly states that "only the court en banc may overrule a binding precedent." Federal Circuit case law also states the rule that a second panel may not overrule a first panel—only a court *en banc* may overrule the decision of a prior panel. See George E. Warren Corp. v. United States, 341 F.3d 1348, 1351 (Fed. Cir. 2003) ("We cannot simply overrule the *Texport* decision, even if we were persuaded ... that it is appropriate; to overrule a precedent, the court must rule en banc."). See also Newell Cos. v. Kenney Mfg. Co., 864 F.2d 757, 765 (Fed. Cir. 1988) ("This court has adopted the rule that prior decisions of a panel of the court are binding precedent on subsequent panels unless and until overturned en banc," even when there is direct conflict between two panel decisions); Kimberly-Clark Corp. v. Fort Howard Paper Co., 772 F.2d 860, 863 (Fed. Cir. 1985) ("Counsel is apparently unaware that a panel of this court is bound by prior precedential decisions unless and until overturned *en banc*.").

Because Pfizer was a panel decision, it could not have overruled the prior panel decision of Glaxo. Furthermore, because an *en banc* hearing in Pfizer was denied, the decision in Pfizer will not overrule Glaxo at some point in the future. Therefore, Glaxo has not been overruled by Pfizer and remains binding precedent. The USPTO therefore improperly ignored the

[1] "Hatch-Waxman Act" refers to the Drug Price Competition and Patent Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

precedential value of Glaxo in determining the eligibility of the '771 patent for patent term restoration.

3. Glaxo Is Distinguishable from Pfizer

a. The Glaxo Case

Glaxo is concerned with the meaning of "product" in the context of eligibility under 35 U.S.C. § 156(a) (the "eligibility section"). Specifically, Glaxo sought a patent term extension under 35 U.S.C. § 156 of US 4,267,320 (the "'320 patent"), which claimed cefuroxime axetil, which was marketed as CEFTIN® tablets. Cefuroxime axetil is an ester of cefuroxime; cefuroxime had never been approved for marketing or use by the FDA. Glaxo also owned US 3,974,153 (the "'153 patent"), which claimed cefuroxime and its salts. Glaxo already marketed two salts of cefuroxime as ZINACEF® and KEFUROX®, approved by the FDA for intramuscular and intravenous administration. Neither of the salts in ZINACEF® nor KEFUROX® is a salt of cefuroxime axetil. Based on the FDA review period for cefuroxime axetil, Glaxo sought extension of the '320 patent term, which was denied because of the previously approved cefuroxime salts. The district court overturned the USPTO's decision finding it "contrary to law" and the Federal Circuit affirmed.

The Federal Circuit in Glaxo concluded that the statutory language of 35 U.S.C. § 156(f)(2) was unambiguous; the terms "active ingredient," "salt," and "ester" all had well-defined, ordinary plain meanings at the time the statute was enacted. Glaxo, 894 F.2d at 395; see, e.g., 45 Fed. Reg. 72,582, 72,591 (1980); 44 Fed. Reg. 2932, 2937-38 (1979). The Court rejected Commissioner Quigg's proposed definition of "product," as being a "new chemical entity," i.e., "new active moiety," because that term also had a well-defined, ordinary plain meaning at the time the statute was enacted (see, e.g., 21 C.F.R. § 314.108(a))[2] and was therefore available to Congress if it had wanted "product" to be so defined. Glaxo, 894 F.2d at 397. In addition, nothing in the legislative history of 35 U.S.C. § 156 suggested a clearly expressed legislative intent contrary to the plain meaning of "active ingredient . . . including any salt or ester of the active ingredient." Id. at 400.

b. The Pfizer Case

Unlike Glaxo, Pfizer is concerned with the scope of claims of an extended patent in the context of enforcement under the "rights derived section" of 35 U.S.C. § 156(b). Specifically, Pfizer owned US 4,572,909 (the "'909 patent"), which claimed amlodipine and its salts. Pfizer, 359 F.3d at 1363. Pfizer submitted to the FDA clinical data for both the besylate and the maleate salts of amlodipine although, in the end, Pfizer only pursued approval of the besylate salt. Id. at 1363-1364. After obtaining FDA approval for amlodipine besylate to be marketed as NORVASC®, Pfizer successfully sought patent term restoration for the '909 patent, and the extended term was based on the time spent on studies on both salts. Id. at 1364. Dr. Reddy's subsequently filed a "paper NDA" under 21 U.S.C. § 355(b)(2) for the maleate salt, also covered by the '909 patent, based on the clinical data Pfizer had submitted to the FDA. Id. Dr. Reddy's

[2] "Active moiety means the molecule ... responsible for the physiological or pharmacological action of the drug substance."

therefore relied on the safety and efficacy data submitted to the FDA by Pfizer for both maleate and besylate salts in seeking approval to market a generic version of Norvasc.

Dr. Reddy's argued that the extension of the '909 patent term should have been limited to only the approved product, namely the amlodipine besylate, not the unapproved maleate salt. Id. Even though both salts are part of the amlodipine "active moiety," as they must be in order for Dr. Reddy's to reference Pfizer's approved application, Dr. Reddy's argued that only the specific salt for which Pfizer obtained approval was protected by the extended term of the patent under 35 U.S.C. § 156(b). In contrast, Pfizer argued that the statute contemplated that a therapeutic product could be administered as a "salt or ester of the active ingredient" and that therefore, an extension could not be defeated simply by changing the specific salt or ester. Id. at 1365.

The Federal Circuit held that the only limitation in the "rights derived section" was to any approved use of the drug product so that the extended patent term would not encompass non-pharmaceutical uses. Pfizer, 359 F.3d at 1366; see also H.R. Rep. No. 98-857, 1984 U.S.C.C.A.N. at 2672; H.R. Rep. No. 97-696 at 10 (1982); 66 J. Pat. Off. Soc'y 525, 528 (1984). Moreover, the Court found that the "rights derived section" did not "contain any limitation regarding the form of the product subject to the extension." Id. Accordingly, the Court concluded that the active ingredient was amlodipine, whether administered as a maleate salt or besylate salt, and that it was undisputed that Dr. Reddy's product was for the same use as the approved use of Pfizer's product. Accordingly, "drug product," in the context of enforcement, means "active moiety," and any "rights derived" from a patent term extension will include an extension of rights for the active moiety, including any salt or ester, and any of its approved uses. As stated by the Federal Circuit, "the text of the statute shows that it was not intended to be defeated by simply changing the salt," Pfizer, 359 F.3d at 1366. In fact, the Federal Circuit expressly referred to this as a loophole that was addressed by Congress in its Section 156(f) definition of "product." Id.; see also 21 U.S.C. § 355(j)(5)(D)(i) and (v). The Federal Circuit concluded that the extended term of the '909 patent covers "amlodipine and any salt or ester, as provided by § 156(f)."

c. Glaxo and Pfizer Are Consistent and Distinguishable from Each Other

A proper reading of Glaxo and Pfizer demonstrates that the two opinions are not inconsistent as the USPTO suggests. Although it may be argued that these opinions construe the term "product" with varying degrees of scope, Glaxo was determined in the context of patent term extension eligibility under 35 U.S.C. § 156(a) while Pfizer was determined in the context of the "rights derived section" of 35 U.S.C. § 156(b). The Court in Pfizer noted the difference between the two sections when it pointed out that § 156(b) did not contain the same limitation as § 156(a), namely, the "approved product," relied on by the district court. Indeed, the Federal Circuit deemed it "unsound" to limit the extension to the "approved product" under the "rights derived section." Id. at 1366.

It is telling that the Pfizer Federal Circuit panel ignores the earlier Glaxo decision because the district court decision, as well as the Federal Circuit briefing and oral argument, all addressed Glaxo. (See, e.g., Brief for Plaintiff-Appellant Pfizer, Inc. at 52; Brief for Defendants-Appellees Dr. Reddy's Laboratories, Ltd. & Dr. Reddy's Laboratories, Inc. at 26, 59.) Had a

conflict between these opinions actually existed, the Federal Circuit likely would not have denied an *en banc* hearing in the Pfizer case, which would have provided the Federal Circuit an opportunity to settle any inconsistency between the cases. Because the Federal Circuit's denial of an *en banc* hearing implies that the two opinions are not in conflict, each should be read as distinguishable from the other so as to avoid any inconsistencies. See Kimberly-Clark, 772 F.2d at 863 ("[S]tatements in opinions of this court must be read harmoniously with prior precedent, not in isolation.").

The USPTO attempts to link the statute's eligibility requirements to the enforcement rights derived from a patent term extension, but by doing so forces an inconsistency upon the law that does not exist.[3] Believing that it is forced to choose between one of two conflicting opinions, the USPTO chooses the later rendered decision (even though in violation of Federal Circuit law, which requires the earlier of two conflicting panel opinions to control) and broadly defines "product" as "active moiety," the very position taken by USPTO Commissioner Quigg in the Glaxo case and flatly rejected by the Federal Circuit in the eligibility context. As explained above, however, no actual inconsistency exists. Pfizer does not interpret "product" for purposes of eligibility but for enforcement and Glaxo does not interpret "product" for purposes of enforcement but for eligibility, but more importantly, the scope of a patent term extension cannot be construed using the same analysis as that used to determine a patent's eligibility for term extension.

4. Under Glaxo, Patent Term Extension of the '771 Patent Should be Granted

As between these two *consistent* decisions of the Federal Circuit, Glaxo applies to eligibility for patent term extension, which is the issue here. Under Glaxo, the '771 patent is entitled to a patent term extension.

The applicable criteria for determining whether an approved product (and the patent for which extension is sought) would be eligible for patent term extension are set forth in section 156(a) as follows: (1) the patent must be unexpired and must not have a term that has been previously extended (35 U.S.C. § 156(a)(1)-(2)); (2) the product was subject to a regulatory review before its commercial marketing or use (35 U.S.C. § 156(a)(4)); (3) the product must represent the first permitted commercial marketing or use of the product (35 U.S.C. § 156(a)(5)); and (4) the application for the patent term extension must be submitted to the USPTO within 60 days of FDA approval of the commercial marketing application (35 U.S.C. § 156(d)(1)). The statute defines "product" to be a "drug product," 35 U.S.C. § 152(f)(1), which is defined as the "active ingredient of a new drug . . . , including any salt or ester of the active ingredient . . . ." 35 U.S.C. § 156(f)(2).

It is not disputed that at least three of these four requirements are satisfied by esomeprazole sodium (marketed under the trade-name NEXIUM® I.V.). First, the '771 patent covers esomeprazole sodium and has a term that is unexpired and has not been extended. Second, the NDA for esomeprazole sodium was subject to regulatory review prior to its commercial marketing or use. Finally, the application of the patent term extension of the '771

[3] In its denial of patent term restoration, the USPTO states: "Eligibility for patent term extension must be consistent with the rights derived from a patent term extension."

patent was submitted to the USPTO within 60 days of the FDA approval of the commercial marketing application for esomeprazole sodium. The only requirement in dispute is whether esomeprazole sodium represents the first permitted commercial marketing or use of the "product" as defined by 35 U.S.C. § 156(f). See also 37 CFR § 1.710 (2005).

The facts surrounding NEXIUM I.V. and the '771 patent are similar to the facts of Glaxo. In both, the drug compound serving as the basis for the patent term extension is covered by a different patent from the patent covering the previously approved drug compounds of the same active moiety. Here, the non-salt, non-ester form of esomeprazole has not been approved by the FDA, just as the non-salt, non-ester form of cefuroxime had not been previously approved by the FDA. In both, the drug compound serving as the basis for the patent term extension is not a salt or ester of any of the previously approved drug compounds. In both, the drug compound serving as the basis for the patent term extension was approved for a dosage form different from the dosage forms approved for the previously approved drug compounds, i.e., esomeprazole sodium was approved by the FDA for intravenous administration and esomeprazole magnesium was previously approved for oral administration. Similarly, in Glaxo, cefuroxime axetil was approved by the FDA for oral administration and the previously approved cefuroxime salts were approved for intramuscular and intravenous administration. Finally, in both situations, the USPTO had originally rejected patent term extension on the basis of a previously approved salt of the same active moiety.

Glaxo's plain meaning interpretation of "*any* salt or ester" supports the proposition that two different salt forms of a therapeutically active substance constitute separate "products" under 35 U.S.C. § 156(f)(1) for the purposes of eligibility for patent term extension. The USPTO has correctly acknowledged that NEXIUM esomeprazole magnesium and NEXIUM I.V. esomeprazole sodium are different and separate active ingredients. (Notice at 1.) According to Glaxo, because the terms of the definition of "product" in 35 U.S.C. § 156(f) are unambiguous and are to be accorded their plain meaning, an active ingredient, and therefore a "product," can be in either a non-salt, salt or ester form. In other words, each form of the active ingredient is a separate "product" for purposes of eligibility under 35 U.S.C. § 156(a).[4] Accordingly, NEXIUM I.V. contains an active ingredient, i.e., esomeprazole sodium, never before approved by the FDA and thereby satisfies all of the requirements for a patent term extension.

The Court in Glaxo specifically rejected the argument made by Commissioner Quigg, now repeated by the USPTO in its rejection of Astra Zeneca's instant application, that, for eligibility, the term "active ingredient" encompasses an entire active moiety including all of the salts and esters of a therapeutically active compound. Commissioner Quigg had suggested that the definition of "product" means "new chemical entity," i.e., "new active moiety," which would include all acid, salt or ester forms of a single therapeutically active substance. Glaxo, 894 F.2d at 394. Quigg's position was that regardless of the form with which a therapeutically active substance is administered, it is metabolized to the same substance. Following Quigg's line of reasoning, the USPTO argues that "if the rights derived from the extension of a patent based

[4] The USPTO incorrectly states the conclusion of Glaxo as follows: "In Glaxo, the court found that since the new member . . . was neither a salt nor an ester of a previously approved product, the new ester could support a patent term extension." Even if this interpretation were correct, esomeprazole sodium would still be eligible for a patent term extension because it is neither a salt nor an ester of any previously approved product. The only other approved form of esomeprazole is its magnesium salt; esomeprazole sodium is not a salt of esomeprazole magnesium.

upon the regulatory approval of a salt encompass other compounds within the same active moiety, then extension based upon subsequent approvals of other compounds within the same active moiety must be barred." (Notice at 3.) Just as the Federal Circuit rejected this "active moiety" argument in Glaxo, so should it be rejected here.

Not only does Pfizer not apply to the eligibility issue presented by AstraZeneca's instant applications, but it is also distinguishable from the current application for several other reasons. Here, data for esomeprazole sodium was not included in pivotal studies (supporting clinical safety and efficacy) in the NDA for esomeprazole magnesium. Each of the marketed drugs was approved by the FDA based on separate NDAs containing data from separate clinical trials. In Pfizer, however, the Federal Circuit was presented with Pfizer's branded product and Dr. Reddy's FDA application that sought to rely on Pfizer's data for approval of a different salt from the approved salt form. In other words, Dr. Reddy's was merely a second manufacturer seeking to take advantage of a purported loophole, the existence of which the Federal Circuit rejected. Pfizer, 359 F.3d at 1366.

Significantly, here there is no attempt to avoid a previously approved patent term extension to avoid infringement by designing around a previously approved product. Both NEXIUM and NEXIUM I.V. are innovator drug products marketed by the same drug company. Furthermore, NEXIUM I.V. is a different dosage form from the previously approved oral dosage form for esomeprazole magnesium. NEXIUM I.V. is not merely an exchange of sodium salt for magnesium salt, all covered by one patent and administered in the same tablet form, but instead is a novel drug product in a new dosage form for which a separate patent was granted and for which a separate NDA was submitted.

Accordingly, Pfizer should not affect the eligibility of NEXIUM I.V. for patent term extension. As Glaxo is the Federal Circuit decision that is applicable to the eligibility of the '771 patent for patent term restoration, the meaning of "product" according to the analysis used in Glaxo should guide the USPTO's determination here. Esomeprazole sodium is a salt of esomeprazole never before approved and is therefore entitled to a patent term extension under 35 U.S.C. § 156(a) as interpreted by Glaxo.

5. Policy Rationale Favors Extension of the '771 Patent

The Hatch-Waxman Act (the "Act") was designed to balance the interests of drug innovators with the interests of generic drug producers. First, the Act attempts to increase innovation and encourage new drug research and development by restoring some of the patent term lost while drug products undergo testing and await lengthy FDA pre-market review and approval. See, e.g., H.R. Rep. No. 98-857, 1984 U.S.C.C.A.N. at 2647, 2648, 2650, 2651, 2670. Furthermore, as stated in Glaxo, "Congress clearly had articulated policy reasons for making more types of patents eligible for extension, including to encourage research." Glaxo, 894 F.2d at 396. Second, the Act attempts to increase the availability of low-cost drugs by expanding generic drug approval procedures and benefits to generic producers. See, e.g., H.R. Rep. No. 98-857, 1984 U.S.C.C.A.N. at 2647, 2647-2648. In exchange for granting innovators more time to exploit their patents for new drugs that require lengthy regulatory reviews by providing for extensions of patent terms, generics are permitted to base their generic drug approvals on

previous trials and data submitted by the innovator drug companies even before the patent terms on those innovator drugs have expired. Pfizer, 359 F.3d at 1364, 1365.

The factors supporting the policy rationale of Pfizer on the scope of the "rights derived" from an extended patent term are not present here. In Pfizer, the generic producer attempted to exploit its ability to access the innovator's clinical data for an unapproved salt of a drug compound, without authorization, while at the same time it sought to bar the extension of the innovator's patent coverage. Here, because the issue relates to patent term extension eligibility and not enforcement, the potential for exploitation of the statute by a generic producer is irrelevant.

Whereas extension of the '771 patent term will not harm a generic producer's interests under the Act, its denial will harm the interests of the innovator drug company. The FDA has recognized AstraZeneca's esomeprazole sodium drug product to be an innovative drug separate and distinct from its esomeprazole magnesium drug product. Approval of the esomeprazole sodium product required its own NDA and its own lengthy regulatory review separate and apart from the approval for the esomeprazole magnesium drug product. The use of the newer sodium salt, therefore, is not merely an exchange of one salt for another simply to achieve an otherwise unwarranted patent term extension. It is an innovative step in the research and development process that the Act was designed to encourage.

6. Petition for Extension of Time

AstraZeneca herewith petitions the Commissioner for Patents to extend the time for this Request in response to the Notice of Final Determination, mailed July 28, 2005, for four (4) months from September 28, 2005, to January 28, 2006. Authorization is given to charge the corresponding extension of time fee pursuant to 37 C.F.R. § 1.136(a), and any other required fee in connection with this communication, to Deposit Account No. 23-1703. Any deficiency or overpayment should be charged or credited to the above numbered deposit account.

Respectfully submitted,

Dated: January 27, 2006

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